REMARKS

Claims 1, 2, 4, 8, 10, 11, 13 to 16, 20 to 22 and 26 to 30 as set forth in Appendix II of this paper are herewith presented for further prosecution in this case. Relative to the version of claims previously before the Examiner, Claims 27 to 30 have been added as indicated in the listing of the claims.

New Claims 27 and 29 have been added to further bring out the embodiments of the particles defined in Claims 1 and 26 in which the active ingredient is a compound of formula I,[2] and new Claims 28 and 30 have been added to further bring out the embodiments of the particles defined in Claims 1 and 26 in which the active ingredient is 4-[[4-(2,4,6-trimethylphenyl)amino]-2-pyrimidyl]amino-benzonitrile.[3] Additionally, applicants have amended the table on page 15 of the application to restore the original disclosure thereof. No new matter has been added.

The Examiner objected to the specification taking the position that applicants' amendment of September 01, 2006, introduced new matter within the meaning of Section 132(a). Withdrawal of the respective objection is respectfully solicited in light of the enclosed revision of page 15 of the application which restores the original wording. Favorable action is solicited.

The Examiner rejected Claims 1, 2, 3, 4, 8, 10, 11, 13 to 16 and 20 to 22 under 35 U.S.C. §103(a) as being unpatentable in light of the teaching of ***Andries et al.*** **(US 6,197,779)** when taken in view of the disclosures of ***Goertz et al.*** **(US 4,801,460)**, ***Nakamichi et al.*** **(US 5,456,923)**, ***Sasatani et al.*** **(US 5,876,760)**, ***Takeda*** **(US 5,350,741)** and ***Baert et al.*** **(EP 872 233)**, and rejected Claim 26 under 35 U.S.C. §103(a) as being unpatentable in light of the foregoing combination of prior art when further taken in view of the disclosure of ***Jones et al.*** **(US 4,917,900)**.

In particular, the Examiner argued *"The evidence of record shows that the subject matter as claimed is a combination of known components selected for their known properties. A claim which unites ele-*

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2) Cf., e.g., page 1, indicated line 10, to page 2, indicated line 41, of the application.

3) Cf., e.g., page 14, indicated lines 2 5and 26, of the application.

ments with no change in their respective functions to yield a predictable result is not patentable in the absence of secondary considerations" citing the Supreme Court's statements

> *For over a half century, the [Supreme] Court has held that a "patent for a combination which only unites old elements with no change in their respective functions ... obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men." Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152 [87 USPQ 303] (1950). This is a principal reason for declining to allow patents for what is obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.*[4)]

Applicants respectfully disagree with the Examiner's position that the record supports that applicants' invention is no more than a selection of known ingredients *"for their known function."* The Supreme Court's statement in *Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp.* is therefore not deemed to be applicable. Moreover, the Supreme Court's explanation in *KSR Int'l v. Teleflex Inc.* that *"[t]he combination of familiar elements according to known methods* is likely to be obvious *when it does no more than yield predictable results"*[5)] is deemed to emphasize that a combination of known elements cannot be regarded as being per se obvious. A determination of patentability under 35 U.S.C. §103 should be made upon the facts of the particular case in view of the totality of the circumstances,[6)] and the use of per se rules is improper for determining whether claimed subject matter would have been obvious under 35 U.S.C. §103.[7)] Also, it is well-settled that the prior art references must be read as a whole for what they reasonably teach one of skill in the art, and that it is not proper under a 35 U.S.C. §103(a) analysis to pick and choose among individual parts of cited prior art references *"as a mosaic to recreate a facsimile of the claimed invention."*[8)]

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4) *KSR Int'l v. Teleflex Inc.*, 82 USPQ2d 1385, 1395 (2007).

5) Id., emphasis added.

6) See, e.g., *In re Dillon*, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (in banc).

7) See, e.g., *In re Brouwer*, 77 F.3d 422, 425, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996); *In re Ochiai*, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995); *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994).

8) *Akzo N.V. v. U.S. International Trade Commission*, 1 USPQ2d 1241, 1246 (Fed.Cir. 1986) cert. denied, 482 U.S. 909 (1987)

The Examiner applied the teaching of ***Andries et al.*** to show that compounds in accordance with applicants' formula (I) were known in the art and for stating that such compounds may be formulated in compositions usually employed for systemically administering drugs.[9)]

The disclosures of ***Goertz et al.***, ***Nakamichi et al.***, ***Sasatani et al.***, ***Takada***, ***Baert et al.*** and ***Jones et al.*** were used by the Examiner for allegedly showing that the combination of components and elements of applicants' particles which provide for the specific preparation of the active ingredient qualified as a composition usually employed for systemically administering drugs. Applicants respectfully disagree.

The disclosures of ***Sasatani et al.***, ***Takada***, ***Baert et al.*** and ***Jones et al.*** clearly address special preparations each of which is specifically adapted to provide a formulation for a single particular drug, namely

- pranlukast in the case of ***Sasatani et al.***,
- peptides and proteins in the case of ***Takada***,
- loviride in the case of ***Baert et al.***, and
- zidovudine in the case of ***Jones et al.***

Therefore, neither one of these references can be deemed to describe a formulation which is usually employed for the administration of drugs which differ from the particular active ingredients which are addressed in each of the references. Moreover, pranlukast, peptides, proteins, loviride and zidovudine are materially different from the compounds which are addressed in the teaching of ***Andries et al.*** or the compounds which are represented by applicants' formula (I).

Furthermore, the disclosures of ***Sasatani et al.***, ***Takada***, ***Baert et al.*** and ***Jones et al.*** are deemed to clearly corroborate that a person of ordinary skill in the pertinent art cannot reasonably expect that the results and properties of a formulation of one particular drug such as, for example, pranlukast may suggest or imply any results or properties which may be obtained when pranlukast is replaced, for example, by loviride. The Examiner will note that ***Sasatani et al.*** inter alia provide that spray-drying of a mixture of water, a water-soluble polymer, lactose and pranlukast yielded granules comprising crystals of pranlukast,[10)] whereas ***Baert et al.*** describe that solid

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9) Cf., e.g., col. 18, indicated lines 19 to 43, of ***US 6,197,779***.

10) Cf. col. 6, indicated lines 34 to 48, and col. 4, indicated lines 24 to 31, of ***US 5,876,760***.

dispersions of loviride may be obtained either by way of melt extrusion or by way of spray-drying of certain mixtures comprising a water-soluble polymer and loviride.[11] Of course, the only similarity between the respective preparations resides in the fact that each group of authors inter alia employ a water-soluble polymer.[12] It has to be appreciated, however, that ***Sasatani et al.*** use the water-soluble polymer as an alternative to a surfactant to improve the wettability and dispersibility of the pranlukast crystals,[13] whereas ***Baert et al.*** employ the water-soluble polymer as a polymer matrix. In contrast to either one of ***Sasatani et al.*** and ***Baert et al.***, ***Jones et al.*** employ at most 20% by weight of a water-soluble polymer as a binder for compositions comprising at least 80% by weight of zidovudine,[14] and ***Takada*** merely mentions the water-soluble polymer polyvinylpyrrolidone among optional excipients in an enteric preparation of peptides and proteins.

On the one hand, the references clearly corroborate that the usefulness of a particular preparation for one type of active ingredient cannot be deemed to suggest or imply that the preparation is useful for another and materially different type of active ingredient. On the other hand, the disclosures of ***Sasatani et al.***, ***Takada***, ***Baert et al.*** and ***Jones et al.*** are therefore also deemed to corroborate that the usefulness of a water-soluble polymer in a formulation of an active ingredient depends on the nature of the active ingredient which is to be formulated. A person of ordinary skill in the pertinent art having the disclosures of ***Sasatani et al.***, ***Takada***, ***Baert et al.*** and ***Jones et al.*** before him, therefore, cannot reasonably predict whether a water-soluble polymer may be a useful ingredient in the context of a formulation of an active ingredient such as disclosed by ***Andries et al.*** or as encompassed by applicants' formula (I). As such, the references clearly cannot be deemed to show that the claimed combination of elements is no more than *"a combination of known components selected for their known properties"* as the Examiner would have it.

An inclusion of the disclosure of ***Goertz et al.*** and of ***Nakamichi et al.*** into the contemplation is not deemed to alter the result.

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11) E.g., page 3, indicated lines 48 to 53, of ***EP 872 233***.

12) E.g., col. 3, indicated lines 34 to 43, of ***US 5,876,760***, and page 4, indicated lines 10 to 32, of ***EP 872 233***.

13) E.g., col. 3, indicated lines 39 to 41, of ***US 5,876,760***.

14) E.g., col. 3, indicated line 56, to col. 4, indicated line 2, of ***US 4,917,900***.

Although both ***Goertz et al.*** and ***Nakamichi et al.*** address the preparation of solid solutions or dispersions of pharmaceutically active ingredients,[15] neither one of the references refers to or suggests active ingredients of the type addressed by ***Andries et al.*** or encompassed by applicants' formula (I). Moreover, the preparations are not deemed to be sufficiently similar to each other, or to the formulations of ***Sasatani et al.***, ***Takada***, ***Baert et al.*** and ***Jones et al.***, to support that a person of ordinary skill in the pertinent art could reasonably expect alternative embodiments of elements of ***Nakamichi et al.***'s preparation, or of the formulations of ***Sasatani et al.***, ***Takada***, ***Baert et al.*** and ***Jones et al.***, to be suited in the context of the disclosure of ***Goertz et al.*** At the time applicants made their invention it was even less predictable whether one of the prior art preparations, or a modification thereof, was suited as a composition for administering the compounds of ***Andries et al.***

Goertz et al. disclose a process in which active ingredient is mixed with an NVP polymer which serves as a fusible binder, and optionally with other conventional auxiliaries, at from 50 to 180°C, and the mixture is subjected to injection molding or extrusion and shaping.[16] Additionally, ***Goertz et al.*** inter alia specifically require, on the one hand, that the NVP polymer be solvent-free and that the polymer have a water content of not more than 3.5% by weight,[17] and, on the other hand, that the mixture do not contain any thermoplastics which are sparingly soluble in gastric juice, i.e., enteric polymers.[18]

In contrast thereto, ***Nakamichi et al.*** provides for preparations which may be based on virtually any natural or synthetic polymer, including pH-dependent polymers, pH-independent polymers and water-soluble polymers, and that such polymers may be used independently or in a combination of two or more species.[19] Notably, the list of illustrative polymers which is provided by the authors in this context includes a number of enteric polymers, i.e., polymers which are specifically mentioned by ***Goertz et al.*** as being unsuited in the context

15) E.g. col. 1, indicated lines 5 to 8, of ***US 4,801,460***, and col. 1, indicated lines 8 to 16, of ***US 5,456,923***.

16) E.g., col. 1, indicated line 64, to col. 2, indicated line 3, of ***US 4,801,460***.

17) E.g., col. 2, indicated lines 4 to 6, and col. 3m indicated lines 20 to 31, of ***US 4,801,460***.

18) E.g., col. 2, indicated lines 14 to 16, and col. 3, indicated lines 20 to 31, of ***US 4,801,460***.

19) E.g., col. 2, indicated lines 32 to 61, of ***US 5,456,923***.

of their preparation.[20] It is deemed to be immediately apparent that any equivalence of the polymeric materials which are enumerated by ***Nakamichi et al.*** cannot reasonably be expected to apply in the context of the preparations of ***Goertz et al.*** Also notably, the illustrative preparations according to ***Nakamichi et al.***'s disclosure are without exception obtained under addition of aqueous solutions or water,[21] or with solvent,[22] rather than in a solvent-free manner without the addition of water as is specifically required in accordance with ***Goertz et al.***'s disclosure. These differences further corroborate that a person of ordinary skill in the pertinent art could not reasonably expect that measures which may be suitable in accordance with the disclosure of ***Nakamichi et al.*** may be successfully employed in the context of ***Goertz et al.***'s disclosure.

Similar considerations apply with regard to the disclosure of ***Sasatani et al.*** in combination with either one or both of ***Goertz et al.*** and ***Nakamichi et al.*** For example, ***Sasatani et al.*** particularly distinguish their preparation from the solid solutions or dispersions which are addressed by ***Goertz et al.*** and ***Nakamichi et al.***, pointing out that the drug, i.e., pranlukast, is present in the preparation in the state of solid crystals rather than in a molecular dispersed or dissolved form.[23] ***Sasatani et al.***'s disclosure addresses a method of modifying the surface adhesiveness of pranlukast crystals in which a water soluble polymer and/or a surfactant is employed in a suspension with water and optionally organic solvents to improve the wettability and dispersibility of the crystals.[24] On the one hand, the reference clearly corroborates that a combination of a water-soluble polymer and a drug does not necessarily comprise the drug in a molecular dispersed or dissolved form. On the other hand, it should be noted that the reference describes the water soluble polymer and the surfactant as being equivalents in the context of the particular pranlukast preparation. Such an equivalence can clearly not be alleged to be present or reasonably expectable in the context of the preparations which are disclosed by ***Goertz et al.*** and/or ***Nakamichi et al.*** A

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20) Cf. col. 2, indicated lines 42 to 59, of ***US 5,456,923*** and, e.g., col. 4, indicated lines 4 to 20, of ***US 5,350,741***.

21) Cf. col. 6, indicated line 30, to col. 8, indicated line 27, of ***US 5,456,923***.

22) Cf. col. 8, indicated line 29, to col. 9, indicated line 24, of ***US 5,456,923***.

23) Col. 4, indicated line 26 to 31, of ***US 5,876,760***.

24) Col. 3, indicated lines 34 to 43, and col. 5, indicated lines 11 to 17, of ***US 5,876,760***.

person of ordinary skill in the pertinent art therefore could not reasonably expect that surfactants and/or other ingredients which are suitable in the context of ***Sasatani et al.***'s preparation may also be successfully employed in the context of ***Goertz et al.***'s and/or ***Nakamichi et al.***'s preparation.

The disclosure of ***Takada*** pertains to enteric formulations of active peptides and proteins, i.e., substances which are neither addressed nor suggested in the disclosures of ***Goertz et al.***, ***Nakamichi et al.*** or ***Sasatani et al.*** Similar to the disclosure of ***Sasatani et al.***, ***Takeda*** prepares the formulations from solutions and the formulations, therefore, cannot be deemed to resemble the solid dispersions and solutions of ***Goertz et al.*** and/or ***Nakamichi et al.***

In light of the foregoing reasons and explanations as well as the explanations already presented in with applicants' papers dated May 10, 2005, December 13, 2005, September 01, 2006 and October 31, 2007,[25] it is respectfully urged that the subject matter of applicants' claims is not rendered unpatentable under 35 U.S.C. §103(a) by the teaching of ***Andries et al.*** when taken in view of ***Goertz et al.***, ***Nakamichi et al.***, ***Sasatani et al.***, ***Takeda***, ***Baert et al.*** and ***Jones et al.*** Favorable reconsideration of the Examiner's position and withdrawal of the rejections is respectfully solicited.

25) The respective papers are herewith incorporated by reference.